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THYROID IN PREGNANCY*

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WOMAN in the pregnant state demands considerable activity on the part of her complex endocrine system. It has long been known that the thyroid frequently is enlarged at menstruation and during pregnancy. That there is an actual hyperfunction of the thyroid gland of the mother during pregnancy was recently demonstrated by Soule[1] who found that a substance is present in the blood serum of pregnant women, which lowers the level of mouse-liver glycogen; which reduction indicates an increased level of thyroid hormone. Various observers have estimated the accompanying increase in the rate of metabolism to be from 15 to 25 per cent. The curve ascends slowly until about the sixth month of pregnancy, and thereafter rises more abruptly.

In spite of this increased response of the thyroid to demands of maternal and fetal tissue, true hyperthyroidism is probably never caused by pregnancy, and is not commonly associated with pregnancy. Mussey[2] of the Mayo Clinic stated that exopthalmic goiter is not encountered more than once or twice in 1000 cases of pregnancy in that area, and reported 41 cases of hyperthyroidism occurring over a period of seven years. In the same period of years, Janert[3] reported 18 cases of hyperthyroidism with pregnancy, observed at the Women's Clinic of the New York Hospital, in a total of 23,439 patients; an incidence of only .076 per cent. Wallace[4] found a similar ratio of 9 cases in 11,571 patients admitted to a Brooklyn hospital, while Markee[5] of New York could find only 8 cases of hyperthyroidism with pregnancy in 100,000 admissions. Higher incidences, however, are reported from some of the goiter belt cities. Portis and Roth,[6] found a 1.4 per cent incidence in Chicago, but this was only taking 1000 cases. From Detroit there is a report by Yoakum[7] of a 3.7 per cent incidence. At the Lahey Clinic,[8] out of 3678 consecutive goiter operations, there were only 15 who also were pregnant.

I have recently reviewed 1585 histories of goiter patients admitted to the Los Angeles General Hospital from 1930 to 1940. The diagnosis of coincident nontoxic goiter with pregnancy was given in 19. There were 28 in whom a diagnosis was made of hyperthyroidism with pregnancy. In six of these, the findings were insufficient to be certain of the diagnosis, leaving 22 proven cases. During this same period, the Los Angeles General Hospital admitted 39,419 women who were pregnant, giving an incidence of about .05 per cent of hyperthyroidism in pregnancy, roughly about 1 to 2000.

With but one exception, no treatment was carried out in any of the nontoxic goiters. This one exception was a patient, eight months pregnant, who had to have a thyroidectomy performed because of a huge nodular goiter which was causing grave obstructive dyspnea. She had immediate relief after surgery, and went into labor the same day without further trouble.

Of the 22, five had adenomatous or nodular goiters with an average age of 33 years. The remaining 17 had exopthalmic or diffuse toxic goiters, with an average of 29 years, and of these five, or 30 per cent, were in recurrent exopthalmic goiters. This is certainly a strikingly high percentage of recurrent goiters and would tend to refute the commonly-accepted idea that hyperthyroid patients do not become pregnant. In Lahey's[8] series there were 13 with exopthalmic goiter and two with toxic adenomas, while in Mussey's[2] series there were 29 cases of exopthalmic goiter and 12 of adenomatous goiter.

There is still considerable variation of opinion, not only in this hospital but in others as well, as to what is the course to be advised to the pregnant woman who also has a proven hyperthyroidism. To demonstrate this variation of opinion, I would like to narrate verbatum the notes of the various consultants on one specific case.

REPORT OF CASE

Mrs. R. D., age 26, who had one baby 14 months before, entered the hospital, June, 1932. She complained of nervousness, rapid heart and loss of weight, and felt she might be pregnant, having menstruated last in March, 1932. She had a pulse of 120. The thyroid was enlarged to three times its normal size. She had an exopthalmos and tremor, and the basal metabolic rate was plus 54. She was found to be three months pregnant. Here is what the different consultants had to say:

Consultant No. 1:

"Diffuse hypertrophy of thyroid, probably pregnant, therapeutic abortion would be advisable thing; and then

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take care of thyroid in 10 days or 2 weeks, depending on the patient's condition."

Consultant No. 2:

"Personally, I see no indication for preceding thyroidectomy with abortion. Occasionally, such procedure precipitates crisis, and early in pregnancy, before five months, pregnancy does not add to thyroid toxicity. Spontaneous abortion following thyroidectomy is not common. Tachycardia is, and will persist after abortion."

Consultant No. 3:

"It would be much safer in my opinion to abort the patient expecting some thyroid reaction following, than to remove the thyroid expecting a reaction, with added load of pregnancy."

Consultant No. 4:

"Treat thyroid as indicated. Nothing to be gained by abortion. Review of literature of Mayo, Lahey and other clinics shows that thyroidectomy is operation of choice in these cases, and that pregnancy may be disregarded. Believe thyroidectomy should be done before escape period sets in."

Fortunately in spite of such divergence of opinions among her consultants, this lady finally had a thyroidectomy performed. She made an uneventful recovery, and delivered a healthy baby in December, 1932.

THERAPEUTIC ABORTION

There are those who do favor early therapeutic abortion. At the New York Hospital Women's Clinic,[8] 2.34 per cent of all abortions were for hyperthyroidism, and in no case was thyroidectomy performed. That the thyrotoxicosis, and not the pregnancy should be interrupted, is however, the opinion of the greatest number, among whom are Mussey,[2] Means, Frazier,[9] Bothe,[10] Lahey,[8] and many others. At the Los Angeles General Hospital there were, fortunately, no therapeutic abortions for hyperthyroidism.

COMMENT

Of the five toxic nodular goiters in this study, one had a spontaneous abortion, and one had a hysterectomy of a large fibroid containing a 12 cm. fetus. Another had a spontaneous, eight-months' premature delivery shortly after entrance; one had a thyroidectomy but aborted six weeks later which, therefore, could not have been attributed to the thyroidectomy; and another, admitted at eight months, fibrillating with a heart rate of 160 and a blood pressure of 190, had a quick low Caesarian with normal convalescence, and three months later, thyroidectomy.

As mentioned, five or 30 per cent of diffuse or exopthalmic goiters were in recurrent goiters. The general trend of their management differed so greatly that each should be considered separately. Of the recurrent group, all but one were seen between the second and fourth months of pregnancy, and one at seven months. Thyroidectomy was performed but once and that, in a three months' pregnancy. In another, at two months, surgery was advised but refused, and x-ray therapy was instituted. One was given x-ray therapy in her fourth month, but a follow-up was not possible, and the remaining two were carried along on Lugol's alone. All went to full-term delivery. One receiving x-ray, not being followed to term, wrote in that she was no better. It appears that surgeons are a little bit more hesitant in these recurrent cases.

Of the twelve exopthalmic goiters, seven were admitted in the first trimester. Of these, four had partial thyroidectomy and three were carried along on Lugol's and medical management. Two were not heard from, while the rest all went to full term delivery. There were no operative mortalities. Five exopthalmic goiters were admitted in the seventh or eighth month of pregnancy. These, in the last trimester, were all placed on Lugol's, but only one went on to full-term delivery. All the remaining four had premature deliveries, one had a dead, macerated, seven-month fetus.

DISCUSSION

It is quite obvious from this survey that confusion still exists, and that an attempt should be made to get at least some uniformity of opinion as to what procedure should be carried out in the frank hyperthyroid who is also pregnant.

It has been shown that patients who give some evidence of hyperactivity do better on small doses of iodine during pregnancy. Carl Davis[14] advocates iodine routinely to all pregnant women in goiter belts, and he gives it in the form of one iodostearin tablet every other day, or five drops of Syrup of Hydriodic Acid every other day.

In the mildly toxic cases, medical treatment as advised by Bothe,[10] Mussey[2] and others may be instituted. The patients are placed in bed, given sedatives and Lugol's solution M 10 three times daily after meals, preferably in milk or grape juice. In such cases, however, distinct improvement to normal or near-normal must be reached within two weeks, when it may be decided to carry the patient through pregnancy with iodine. If near or complete remission is *not* obtained within two weeks, partial thyroidectomy should be performed. In these milder cases, medically treated, one must always be mindful of a possibly false sense of security which the first dramatic improvement may produce, only to be followed by a recurrence of symptoms at a later date when surgery might have to be performed at a less favorable period of pregnancy.

Of the frank thyrotoxic case, the words of Lahey are wisdom. He states: "We strongly urge that the association of pregnancy with thyrotoxicosis is distinctly a mortality factor when pregnancy is permitted to advance to the later stages, and that this mortality factor can be avoided without undue risk to mother or pregnancy by early subtotal thyroidectomy." Thyroidectomy in the first trimester does not cause abortion. In Lahey's series the only mother who miscarried, did so after a long automobile ride home from the hospital; and in Mussey's series, there were no miscarriages. The advocates of early interruption

of pregnancy must realize that it leaves the patient *still* with her hyperthyroidism, and that in the presence of hyperthyroidism even a *minor* surgical procedure may throw the patient into a severe crisis.

In the rare case which does not respond to Lugol's solution for preoperative preparation, and in which surgery is considered too great a hazard, one might resort to x-ray therapy. The Hertzler group, of V. E. Chesky, C. R. Schmidt, and W. R. Walsh,[12] has recently done some remarkable work on liver function tests in these cases, and have found alarmingly low liver function in most hyperthyroid states, which can and must be improved by proper glucose replenishment in all of those cases, whether surgery is attempted or not.

The patient who has proceeded into the last trimester with marked hyperthyroidism presents a real problem. The majority will go into premature labor as shown in other series as well as in our own. Mussey[2] states: "Except in selected cases in the last trimester of pregnancy, partial thyroidectomy should be performed if the exopthalmic goiter does not give evidence of complete or nearly complete remission within two weeks after treatment with iodine has begun." Lahey, in his "Surgical Practice" recently published, states: "There need be little change in management of the hyperthyroidism complicated by pregnancy. Operation is advised and carried out up to and including the eighth month." As pregnancy approaches term, one may have reasonable doubt as to what might be the safest procedure. In one very desperate case in this series, a happy result was obtained by a section performed with dispatch. Thyroidectomy at *this* stage almost invariably starts immediate labor process, and one might weigh carefully whether the shock of surgery and delivery all in the period of a day might not prove too much. At this critical period, one might well consider Lugolization and rapid Caesarian rather than prolonged labor.

HYPOTHYROIDISM

The possible rôle of hypothyroidism as a causative factor in amenorrhea, menorrhagia, abortion, miscarriage, premature labor, and death of the fetus has been referred to by Breckenridge,[13] Davis,[11], Frazier and Ulrich,[9] Litzenberg and Carey,[15] and others. Its possible rôle in relationship to toxemia of pregnancy has been pointed out by Hughes,[16] who advises administration of iodine early in pregnancy to those patients who have low metabolic rates. It is his contention that he thereby can reduce the incidence of toxemia later in pregnancy. Although the incidence of sterility is high among hypothyroid women, the fact remains that they do become pregnant.

Myxedema, with its classical thickened skin and fluid retention, should be easily recognized, but other symptoms of hypothyroidism, such as drowsiness, fatigue, joint pains, mental depression, constipation and falling hair might easily be overlooked. In the opinion of Carl Davis,[11] practically all individuals who have a dry skin, slow pulse and a subnormal temperature, have a low metabolic rate. In a series of six hundred consecutive basal metabolic readings in women, he found about 10 per cent with metabolic rates lower than minus 20 to 25, and in his opinion the infants of these women will show a deficiency of thyroid, unless the mothers are given prophylactic doses of thyroid and iodine during pregnancy.

PREVENTION OF GOITER

A presentation of "Thyroid in Pregnancy" would not be complete without mention of something which most obstetricians do not consider in their realm at all, and which they usually relegate into the hands of the pediatrician, namely, that of the *prevention* of goiter. Marine and Kimball,[18] through their epochal work have made those men who take care of children and adolescents, particularly in the goiter belts, very conscious of their duties in the prevention of goiter, and it is almost a universally accepted fact from this work that if the adolescent is given small doses of iodine, endemic goiter can and will be prevented in most cases.

The prevention of goiter goes back even farther, as has been shown by Eggenberger,[17] of Switzerland. He took a large series of pregnant women in one of their large hospitals and gave them all iodine throughout pregnancy. Owing to the use of iodized salt by the prospective mothers from the beginning of pregnancy, in 2,000 cases, no babies were born with goiter. In those cases in whom iodine was not administered, about 50 per cent of the new-born babies showed thyroid enlargement, and 100 per cent epithelial hyperplasia and deficiency of colloid substance in the thyroid gland. Goiter in puberty did not appear in children who used iodized salt from the time of birth. It is evident that the obstetrician and those who do *obstetrics,* particularly in the goiter belts, can play a much greater rôle in the prevention of goiter before birth, than can the pediatrician after birth, by administering iodine routinely to their pregnant women.

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TUMORS OF THE RECTUM*

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TUMORS of the rectum comprise a very large and varied group, and it is not the purpose of this paper to present in outline the various types, but rather to limit the discussion to the polyps or polypoid types of tumors, and especially those that afford evidence of questionable or very frank malignancy.

With rare exceptions these consist of three groups: the benign and malignant adenomas, the villous papillomas, and the carcinomas resembling either the sessile adenoma or, more rarely, the papilloma. The adenomas are true mucosal tumors, and vary in size from tiny, flat, almost invisible growths to tumors of several centimeters in diameter. When small they are sessile, but as they enlarge a pedicle of normal mucosa may or may not be formed by the constant tug on the bowel wall. Histologically, they resemble normal mucosa, except that the glandular structures are more elongated and variable in size. The villous papillomas are soft and sponge-like in appearance and on palpation, usually have a wide base, and may reach a size which fills the ampulla of the rectum.

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BENIGN AND OTHER LESIONS

There has been considerable discussion as to the relationship of the benign rectal polyp to carcinoma of the rectum, and at present it is generally believed that many, if not all of these tumors are definitely premalignant, although it is rare to find high-grade malignancies arising in polyps. Carcinoma of low grade not infrequently may be found in the most innocent-appearing polyps. Of considerable significance is the fact that some of the polyps, in cases of multiple polyposis, almost invariably become malignant, and these are indistinguishable from the ordinary solitary adenoma.

In a series of 827 patients with carcinoma of the colon and rectum, Swinton and Warren[1] demonstrated histologically that 14 per cent had arisen in benign mucosal polyps. Buie and Brust[2] report four patients in whom polyps were found, but were not removed, and in whom carcinomas developed later in the same section of the rectum.

Further support of the belief that the adenoma is a premalignant tumor is found in a study of the age incidence. Martin,[3] Buie and others have shown that the average age of patients with polyps is about ten years younger than the group with carcinoma. Also, their comparative figures of the location of the lesions show a very great similarity.

If it is true that malignancy not infrequently arises in benign polyps, greater efforts should be made to diagnose these tumors early in order that proper treatment may be instituted.

SYMPTOMS

In reviewing the histories of patients with such tumors, the impression is gained that the symptoms do not greatly differ from those of any tumor of the rectum. In fact, there are no symptoms that are diagnostic of any one pathological condition.

When very small, and even when, at times, the polyp reaches considerable size, symptoms referable to the ano-rectal region may be absent, and the presence of the tumor noted on routine proctoscopic examination. This is especially true of the villous papilloma, which may almost fill the rectum yet produce few symptoms.

Bleeding of some type is the most frequent symptom, and may occur before, with or after the stool, and may be mixed with mucus. It may be fresh or altered and may occur in any amount. A change in bowel habits is especially significant of a tumor. In some, tenesmus and the passage of frequent small stools is present, and in others constipation from the obstruction of a large polypoid mass. Pain of a dull, aching character, pain in the back, a feeling of fullness in the rectum or the discomfort of a protruding tumor are not infrequent.

DIAGNOSIS

The diagnosis is made on physical examination and laboratory studies. Examination should consist of a careful, thorough digital examination,